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EXAMINER

MARVICH, MARIA

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/813,156	Applicant(s) SINGH ET AL.	
	Examiner Maria B. Marvich, PhD	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 November 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3,9,13,15,17,21 and 25-69 is/are pending in the application.
- 4a) Of the above claim(s) 25-65 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1,9 and 69 is/are allowed.
- 6) ☒ Claim(s) 3,13 and 66-68 is/are rejected.
- 7) ☒ Claim(s) 15, 17, 21 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 January 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This office action is in response to an amendment filed 11/30/07. Claims 1, 3, 9, 13, 15, 17, 21 and 25-69 are pending in this application. Claims 25-65 have been withdrawn and therefore claims 1, 3, 9, 13, 15, 17, 21 and 66-69 are under examination.

Specification

The disclosure is objected to because of the following informalities: The specification on page 26 contains a partial listing from the sequence listing. For clarity, the sequence listing on pages 26 must be deleted.

On page 2, line 7 the statement "till date" should be amended to --to date--.

Appropriate correction is required.

Election/Restrictions

Newly submitted claims 63-65 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: while the instantly elected claims are drawn to the inducible promoters of SEQ ID NO:1 and SEQ ID NO:2, claims 63-65 are drawn to a method of using the promoter and as such related as product and process of use with the elected invention. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the promoter

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of the elected invention need not be used in the methods of claims 63-65 rather any inducible promoter can be used to induce synthesis of a homologous or heterologous protein.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 25-65 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Objections-minor informalities

Claims 3, 13 and 66-68 are objected to because of the following informalities: For completeness, claim 3 should recite --temperature shift of a culture of cells comprising the promoter--. It is cells comprising the promoter that are subjected to temperature shift and not the isolated promoter itself. This is also the case for claims 66-68.

Claim 13 recites "At least one vector" however the claims that depend from it recite "The vector". It would be remedial to amend claim 13 to recite --A vector-- or to amend the dependent claims to recite --The at least one vector--. Claim 13 also recites "the vector corresponding to Accession No". However, the vector is actually deposited under the Accession number and does not correspond to an Accession number. It would be remedial to recite -- a vector deposited under Accession number --. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 13 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims, as written, do not sufficiently distinguish over cells that exist naturally because the claims do not particularly point out any non-naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty*, 447 U.S. 303,206, USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor., e.g. by insertion of "Isolated" or "Purified". **This rejection is maintained for reasons of record in the office action mailed 8/9/07.**

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3 and 66-68 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for maximum expression of GFP, β -galactosidase, cdc18 or streptokinase within 3 hours of temperature shift from 36°C to 25°C in the absence of thiamine, wherein expression is in *S. pombe* cells transformed with constructs comprising SEQ ID NO:1 or SEQ ID NO:2 operably linked to sequences coding for GFP, β -galactosidase, cdc18 or streptokinase, does not reasonably provide enablement for any other embodiment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

This is a new rejection necessitated by applicant's amendment to indicate that the

promoters of SEQ ID NO:1 and 2 provide maximal expression after 3 hours following temperature shift from 36°C to 25°C.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based on a single factor but is rather a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter, 1986) and *In re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988); these factors include the following:

The instant claims are drawn to promoters and vectors comprising the promoter wherein the promoters consist of SEQ ID NO:2 and 1 comprising 185 and 146 nucleotide fragments of a previously isolated promoter *nmt-1*. Furthermore, the claims are drawn to promoters and vectors further comprising GFP, β -galactosidase, *cdc18*, and streptokinase wherein “said promoter provides maximum expression of GFP (β -galactosidase, *cdc18*, streptokinase) within three hours of temperature shift from 36°C to 25°C”. The instant invention is based upon the advantageous characteristics of the two promoters as they give leaky lower expression, are not deleterious to the cell viability and reduce the level of proteolytic degradation particularly compared to other *nmt* based promoters. However, the claims are drawn to an isolated promoter wherein it is highly unpredictable that maximum expression from the promoter upon temperature shift would be possible in the absence of cells. Rather, induction requires the promoters comprising the operably linked genes to be introduced into *S. pombe* cells prior to transfer to 25°C.

. The specification teaches that genomic DNA was partially digested with *SauI* and clones were isolated. Two such clones exhibited enhanced expression of GFP at 25°C and no expression at 36°C. While the sequences are fragments of the *S. pombe* promoter *nmt-1*, pGFP plasmids containing *nmt-185*, *nmt-146* or *nmt1* promoters, experimentally, the specification demonstrates inductive potential of the promoter wherein *S. pombe* cells transformed with plasmids comprising *nmt-146* and *nmt-185* drive expression of *cdc18*, β -galactosidase, streptokinase and GFP. “It was observed that *nmt1*, *nmt-146* and *nmt-185* promoters were repressed in the presence of thiamine at 36°C as monitored by green fluorescence. However, in absence of thiamine at 36°C, while *nmt1* promoter was derepressed, i.e., GFP gave green fluorescence, the *nmt-185* and *nmt-146* promoter remained repressed, i.e., GFP gene gave no green fluorescence. On the other hand at 25 ° C, *nmt1*, *nmt-185* and *nmt-146* were expressed as indicated by green fluorescence when grown in absence of thiamine. But in presence of thiamine all three promoters were again repressed. Thus, the *nmt-185* and *nmt-146* promoters can be regulated by a temperature shift: they are repressed at 36°C, but expressed upon shift to 25°C in absence of thiamine. In contrast, the *nmt1* promoter is equally expressed at 36°C and 25°C in absence of thiamine.” It is highly unpredictable that in the absence of the cells such maximal expression could be obtained. Furthermore, the specification teaches that the presence of thiamin represses the promoter and hence induction must occur in the absence of thiamine.

The MPEP teaches, “However, claims reading on significant numbers of inoperative embodiments would render claims non-enabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative. *Atlas Powder Co. v. E.I. duPont de Nemours & Co.*, 750 F.2d 1569, 1577, 224 USPQ

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409, 414 (Fed. Cir. 1984); *In re Cook*, 439 F.2d 730, 735, 169 USPQ 298, 302 (CCPA 1971). (see MPEP 2164.08(b). In the instant case, the claims lack critical elements to provide the recited function and given the lack of guidance and disclosure in the specification undue experimentation would be required to identify the proper configurations to provide the exact expression levels. Secondly, the art teaches that nmt-1 promoters are *S. pombe* specific promoters and furthermore that functionality even in related species such as *cerevisiae* and *pombe*, “Fission yeast replication origins, promoters, and splicing mechanisms are all quite different from those in budding yeast. Thus, expression of marker genes is likely to be poor to non-existent. (The notable exception is the *ScLEU2* marker, which works reasonably to complement *SpLeu1*, at least in high copy.) The promoter of your favorite *cerevisiae* gene probably won't work in fission yeast, and it won't be spliced correctly. And in the absence of a *pombe*-specific replication origin, the plasmid will transform inefficiently, if at all, and will be prone to re-arrangement. So how to do cross complementation experiments? the answer is, with a cDNA (or a clone without introns), in a plasmid built for *pombe* --including marker, origin, and promoter driving the cDNA. That way, you can at least be confident your clone expresses and draw a meaningful conclusion from your experiment! Note this also is true for genes from other organisms.” (see the Forsburg Lab *pombe* pages, ¶ 4, Cross complementation).

Response to Argument

Applicants traverse the claim rejections under 35 U.S.C. 112, first paragraph on pages 11-13 of the amendment filed 11/30/07. Applicants' arguments have been fully considered but they are not persuasive. Applicants have not overcome the rejections as set forth above that are

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based upon the inability to induce maximum expression of the isolated promoter operably linked to a gene unless the nucleic acid is in *S. pombe*. As set forth in the appendix applicants have submitted page 655, the DNA is introduced into host cells and expression is mediated by the host cell (see ¶ 3). Applicants have not set forth that maximal expression is achieved in cells other than *S. pombe*. The nmt-1 promoter has only been demonstrated to be functional in *pombe* cells and in these cells demonstrates an inducibility that is maximal 3 hours after temperature shift in the absence of thiamine.

Claim Rejections - 35 USC § 102

Applicants' amendment is persuasive in overcoming the rejection under 35 USC 102.

Conclusion

Claims 1, 9 and 69 are allowable. Claims 3, 13 and 66-68 are rejected.

Claims 15, 17 and 21 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

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the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B. Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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